

REMARKS

In the Final Action, claims 1-3, 9, 12-18 and 20 are pending and under consideration. Claims 1-3, 9, 12-18 and 20 are objected to as containing subject matter drawn to non-elected embodiments. Claims 1-3, 9, 12-18 and 20 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. Claims 1-3, 9, 12-18 and 20 are further rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement. Additionally, claims 1-3, 9, 12-18 and 20 are rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite.

This Response addresses each of the Examiner's rejections and objections. Applicants therefore respectfully submit that the present application is in condition for allowance or at least in better condition for appeal. Favorable consideration of all pending claims is therefore respectfully requested.

Claims 1-3, 9, 12-18 and 20 are objected to as allegedly containing subject matter drawn to non-elected embodiments.

It is believed that the claims, as presently amended, are drawn to elected subject matter, namely, genetically modified non-human animal, which is characterized by reduced levels of Bcl-w protein, as a result of genetic modification of the endogenous *bcl-w* gene.

Claims 1-3, 9, 12-18 and 20 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

The Examiner is of the opinion that the description does not clearly convey to those skilled in the art that a protein having 47% similarity to SEQ ID NO: 4 will have the same function as SEQ ID NO: 4, and will, if expressed at reduced levels, cause a failure of productive

spermatogenesis in non-mouse species of animals or birds. Additionally, the Examiner contends that the specification does not adequately describe a mouse with *decreased* expression of Bcl-w or homologs thereof. While acknowledging the description of a mouse *lacking* Bcl-w and exhibiting an inability to produce sperm, the Examiner contends that the specification fails to describe any other species of animal with reduced levels of any Bcl-w homolog that fails to undergo spermatogenesis as a result of an altered expression.

Applicants respectfully submit that independent claim 1 has been amended to delete the "47% similarity" language and to delineate specifically that the Bcl-w protein is as set forth in SEQ ID NO: 4. The claims have also been amended to specifically recite "homozygous genetically modified male mouse". Applicants reserve the right to pursue the subject matter encompassed by the claims as originally filed in a continuation application.

Applicants further respectfully submit that the present specification not only describes that animals lacking Bcl-w fail to produce sperm, but also describes that animals having reduced levels of Bcl-w would have an incapacity or reduced capacity to undergo spermatogenesis. The relevant description is found, e.g., at pages 8, lines 1-5 of the specification. The Examiner appears to be requiring Applicants to present evidence that such an animal was actually produced. The specification certainly demonstrated, by actual examples, the production of a mouse lacking Bcl-w and exhibiting an inability to produce sperm. The law does not require an actual reduction to practice of every aspect of the claimed invention for the purpose of satisfying the written description requirement. Given the present teaching, those skilled in the art would consider that the specification has conveyed that the Applicants were in possession of the claimed subject matter at the time the application was filed.

Accordingly, Applicants respectfully submit that the written description rejection of Claims 1-3, 9, 12-18 and 20 under 35 U.S.C. §112, first paragraph, is overcome and withdrawal thereof is respectfully requested.

Claims 1-3, 9, 12-18 and 20 are rejected under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement.

In the first instance, the Examiner maintains that the specification does not teach any phenotype for any mouse other than homozygous males. In an effort to favorably advance prosecution, Applicants have amended the claims to recite "homozygous male mouse". Applicants reserve the right to pursue the subject matter encompassed by the claims as originally filed in a continuation application.

The Examiner further maintains that the specification only teaches the phenotype of *incapacity* for spermatogenesis, not a *reduced* capacity for spermatogenesis. Moreover, the Examiner contends that the specification does not teach any (i.e., all) type of genetic modification of the *bcl-w* gene to achieve a reduction of the Bcl-w protein, other than a total lack of the Bcl-w protein.

Applicants respectfully submit that the present application describes how to generate a mutation that results in no active or substantially reduced levels of Bcl-w protein. See, e.g., page 14, lines 9-18. One skilled in the art, based on the teaching of the present invention, combined with techniques well established in the art, can readily make and use transgenic animals with a mutant *bcl-w* gene resulting in a reduced capacity for spermatogenesis, without undue experimentation.

Moreover, the Examiner maintains that the claims encompass a chimeric mouse (genetic mosaics) wherein only a portion of the cells of the mouse contains the claimed genetic disruption. The Examiner is of the opinion that it would take undue experimentation for those skilled in the art to determine the phenotype of a chimeric mouse.

Applicants respectfully submit that the phenotype of a chimeric animal can be readily determined by those skilled in the art, using routine techniques available to those skilled in the art.

Accordingly, it is respectfully submitted that based on the teaching of the present application, those skilled in the art can make a genetically modified male mouse, as claimed, without undue experimentation. Therefore, the rejection of Claims 1-3, 9, 12-18 and 20 under 35 U.S.C. §112, first paragraph, is overcome and withdrawal thereof is respectfully requested.

Claims 1-3, 9, 12-18 and 20 are rejected under 35 U.S.C. §112, second paragraph as allegedly indefinite.

The Examiner maintains that the term "reduced capacity" in claim 1 is a relative term, which renders the claim indefinite. It is respectfully submitted that claim 1 has been amended to include a reference of comparison to non-genetically modified mice.

The Examiner also alleges that claims 2, 3, and 12 are unclear for reciting "at least about". Furthermore, the Examiner alleges that the term "substantially" recited in claims 14 and 20 render the claims indefinite. It is respectfully submitted that the claims, as amended, do not include the terms to which the Examiner has objected.

Moreover, the Examiner contends that claim 1 is unclear, because it appears to encompass an animal that is not genetically modified. It is respectfully submitted that claim 1 has been amended to specifically recite "genetically modified" male mouse.

Additionally, the Examiner contends that it is unclear as to the origin of the relevant Bcl-w protein and its relationship with the animal. Applicants respectfully submit that the genetically modified male mouse, as claimed, exhibits reduced levels of a Bcl-w protein or a functional derivative thereof, as compared to non-genetically modified mice. It is implicit that the Bcl-w protein, recited in the present claims, is endogenous to the genetically modified male mouse.

In view of the foregoing amendments and remarks, it is respectfully submitted that the claims, as amended, are not indefinite. Withdrawal of the rejection under 35 U.S.C. §112, second paragraph, is respectfully requested.

Accordingly, it is firmly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



Xiaochun Zhu
Registration No. 56,311

SCULLY, SCOTT, MURPHY & PRESSER
400 Garden City Plaza-STE 300
Garden City, New York 11530
(516) 742-4343
XZ:ab